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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,206	06/13/2000	RONG FU WANG	2026-4269US1	1577

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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/529,206	WANG ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/16/2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,5-8,10,12-15,26,28,29,67-77,83-85 and 87-103* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,5-8,10,12-15,26,28,29,67-77,83-85,87,88 and 92-103* is/are rejected.

7)☒ Claim(s) *89-91* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-2, 4, 9, 11, 16-25, 27, 30-66, 78-82 and 86 have been cancelled. Claims 26 and 28 have been amended.

2. Claims 3, 5-8, 10, 12-15, 26, 28-29, 67-77, 83-85 and 87-103 are pending and under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections/Rejections Withdrawn

4. The objection of claim 87 for failing to further limit the subject matter of base claim 3 is withdrawn in view of applicant's arguments.

5. The rejection of claims 3, 5-8, 10, 12-15, 26, 67-77 and 87, part a, under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of applicant's arguments.

6. The rejection of claims 10, 12-15 and 69-77 under 35 U.S.C 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention is withdrawn upon further consideration since these claims are drawn to specific cancer peptides of SEQ ID NO:4, which meets the written description requirement.

7. The rejection of claims 10, 13-14, 70-71, 73-77 and 89-91 under 35 U.S.C 112, first paragraph, NEW MATTER, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention is withdrawn upon further consideration since these claims are drawn to specific cancer peptides of SEQ ID NO:4 disclosed in Tables 6 and 7 as-filed.

8. The rejection of claims 10, 13-15, 70-71, 73-77 and 89-103 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn in view of applicant's arguments.

Response to Arguments

9. The rejection of claims 3, 5-8, 10, 12-15, 26, 67-77 and 87, part b, under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained.

The response filed 12/16/2004 has been carefully considered, but is deemed not to be persuasive. The response states that the ordinary skilled artisan understands whether peptides are immunologically recognized by T-cells and the specification provides routine assays in Examples 2, 3, 11-13 and 15 that provide standards for

determining functionally equivalent variants. In response to these arguments, the specification at page 13 defines the phrase "functionally equivalent variants" to include peptides with partial sequence homology, peptides having one or more specific conservative and/or non-conservative amino acid changes, peptide conjugates, chimeric proteins, fusion proteins and peptide nucleic acids. Thus, the phrase encompasses peptides, chimeric proteins and fusion proteins having disparate functions, which function is not clearly defined by the claims. The fact that the "functionally equivalent variant" is recognized by antigen specific cytotoxic T lymphocytes does not clearly set forth the actual function of the "functionally equivalent variant" since recognition by specific cytotoxic T lymphocytes is a property or characteristic of the "functionally equivalent variant". Further, the specification at page 13 does not define the phrase "functionally equivalent variant" in terms of immunological recognition by cytotoxic T lymphocytes. Therefore, the skilled artisan would not reasonably be apprised of the metes and bounds of the invention and thus, the rejection is maintained.

10. The rejection of claims 3, 5-8, 26, 67-68 and 87 under 35 U.S.C 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention is maintained.

The response filed 12/16/2004 has been carefully considered, but is deemed not to be persuasive. The response states that the specification explicitly recites nucleic acids having sequences of positions 55-62 and 127-136 of SEQ ID NO:4 as SEQ ID NOS:31 and 15, which are shown in Tables 6 and 7 and the specification explicitly discloses that portions and variants are within the scope of the present invention (page 9, line 21). Applicant notes that there is no per se requirement to disclose a complete DNA sequence when claiming DNA sequences citing the Office's Guidelines on the Written Description (Fed. Reg., Vol. 66, No. 4, p.1101, comment No. 9 (Jan 5, 2001). The response also states that the structural requirements for function are disclosed in the specification at page 47, lines 4-19 and page 53, lines 4-15 and applicant argues that the claims are not drawn to alleles and any analysis of alleles is irrelevant. In response to these arguments, it is reiterated that the specification at page 9, lines 21-27 discloses that cancer peptides sharing at least 85% sequence homology with the human cancer peptide of SEQ ID NO:4 (NY ESO-1/CAG-3). There is inadequate written description for the homologous cancer peptides from other mammalian sources, including primate and murine homologs, encompassed by the broad claims. Neither the specification's description of exemplary T-cell epitopes from the human cancer peptide of SEQ ID NO:4 (i.e., Tables 6 and 7), nor its general description of how those skilled in the art could find other homologus T-cell epitopes that are at least 85% identical to a cancer peptide that is about 10 amino acids in length and includes amino acids 55-62 of SEQ ID NO:4 or amino acids 127-136 of SEQ ID NO:4 is adequate to describe the genus broadly defined by base claims 3 and 26. One cannot describe what one has not

conceived. See Fiddles v.Baird, 30 USPQ2d 1481, 1483. In Fiddles v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

The instant disclosure only provides adequate written description for the human cancer peptide of SEQ ID NO:4, the disclosure does not disclose the relevant, identifying characteristics such as structure or other physical and/or chemical properties of homologous cancer peptides that share at least 85% sequence homology with the claimed NY ESO-1/CAG-3 cancer peptides that include amino acids 55-62 or 126-137 of SEQ ID NO:4. Furthermore, the characteristic wherein the functionally equivalent variant cancer peptides are recognized by antigen specific cytotoxic T lymphocytes is insufficient to define the genus. Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required. A description of what a material does, rather than what it is, usually does not suffice. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

With respect to the specification at page 9 explicitly disclosing that portions and variants are within the scope of the present invention, adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. With respect to applicant's argument that alleles are not claimed and thus, not relevant, the claim language "functionally equivalent variant has at least 85% sequence homology with the cancer peptide..." broadly encompasses cancer peptides encoded by alternate

forms of a gene or alleles and as such are relevant. It is reiterated that if the structure of the allelic sequences are not defined, the protein product encoded thereby is also not defined and therefore does not meet the written description requirement. Applicant's reference to the written description guidelines is unclear because applicant is not claiming a DNA sequence.

11. The rejection of claims 3, 5-8, 10, 12, 26, 67-69, 72, 87-88 and 92-103 under 35 U.S.C 112, first paragraph, NEW MATTER, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention is maintained.

The response filed 12/16/2004 has been carefully considered, but is deemed not to be persuasive. The response argues that the specification at page 9, line 21 states "[a]lso encompassed in the ambit of the invention are cancer peptides or portions thereof that share partial sequence homology with SEQ ID NO:4. By partial amino acid sequence homology is meant a peptide having at least 85% sequence homology with SEQ ID NO:4..." Applicant refers to Table 7, which discloses sixteen peptides, including some with sequences longer than 10 amino acids, that maintain significant activity (e.g., SEQ ID NOS:26-30). In response to these arguments, the general disclosure at page 9, which includes undefined portions of SEQ ID NO:4, does not provide adequate written support for the narrower limitations of a cancer peptide "about 10 contiguous amino acids of SEQ ID NO:4 that include amino acids 55-62 of SEQ ID

NO:4 or amino acids 127-136 of SEQ ID NO:4..." and functionally equivalent variants thereof having at least 85% sequence homology with said cancer peptide. Again, a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05. Thus, the specification at page 9, which generically describes just any portion of SEQ ID NO:4 does not adequately support the narrower limitations of the present claims, which requires a cancer peptide that is about 10 contiguous amino acid residues and includes amino acids 55-62 or 127-136 of SEQ ID NO:4 and optionally 1 to about 10 or 1 to about 5 (claim 12) additional contiguous amino acids of SEQ ID NO:4 as well as functionally equivalent variants thereof. Where in the specification at page 9, is it contemplated that the cancer peptide "portions thereof" includes amino acids 55-62 of SEQ ID NO:4 or includes amino acids 127-136 of SEQ ID NO:4 and is about 10 amino acids in length as well as peptides having at least 85% sequence homology to said portions?

Applicant also argues that the specification contains more than mere generic disclosure as Tables 6 and 7 disclose nineteen distinct embodiments and that there is no need for applicant to rely on matter that is "obvious" from the disclosure, but not disclosed. In response to this argument, the data provided in Table 7 only provides adequate written description and would have only led the skilled artisan to those particular peptides disclosed and not to the broader limitation of peptide variants having at least 85% sequence homology with the peptide sequences of Table 7 or Table 6 as

presently claimed, particularly in view that many of the sequences disclosed in Tables 6 and 7 were not recognized by cytotoxic T lymphocytes. Further, the claims recite that the cancer peptide is "about" 10 contiguous amino acids of SEQ ID NO:4 and optionally 1 to about 10 or 1 to about 5 additional contiguous amino acids of SEQ ID NO:4. The longest peptide disclosed in Table 7 is 15 amino acids in length (e.g., SEQ ID NO:26). Thus, there is insufficient written support for the present claim limitations of "about" 10 contiguous amino acids of SEQ ID NO:4 and optionally 1 to about 10 or 1 to about 5 additional contiguous amino acids of SEQ ID NO:4, which encompasses peptide that are longer than 20 amino acids in length or longer than those peptides disclosed in Tables 6 and 7. Also, there is insufficient written support for a cancer peptide consisting of amino acids 43-62 of SEQ ID NO:4 (i.e., SEQ ID NO:45) (claim 15) in Tables 6 and 7. Further, Table 6 at page 45 discloses SEQ ID NO:15 (i.e., amino acids 127-136 of SEQ ID NO:4), however, there is no disclosure for the broader recitation of a cancer peptide having at least 85% sequence homology with amino acids 127-136 of SEQ ID NO:4 or even peptide sequences about 10 contiguous amino acids of SEQ ID NO:4 that include amino acids 127-136 of SEQ ID NO:4 and optionally 1 to about 10 or 1 to about 5 (claim 12) additional contiguous amino acids of SEQ ID NO:4. Additionally, the specific amino acid substitutions and amino acid additions at the N-terminus of peptides disclosed in Table 7 does not provide adequate written support for the present broader limitations of just any amino acid substitution at amino acid 54 of the cancer peptide consisting of amino acids 53-62 of SEQ ID NO:4 or just any additional amino acid at the N-terminus

of the cancer peptide consisting of amino acids 54-62 of SEQ ID NO:4 and (i.e., claims 69, 72, 88 and 92-103).

Applicant is reminded that the introduction of claim changes which involve narrowing or broadening the claims by introducing elements or limitations which are not supported by the as-field disclosure is a violation of the written description requirement of 35 U.S.C. 112, first paragraph. MPEP 2163.05.

Applicant is required to cancel the new matter in the response to this Office Action or specifically point out in the as-filed disclosure where written support for all of the instant claim limitations can be found.

12. The rejection of claims 3, 5-8, 12, 26, 67-69, 72 and 87-88 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained.

The response filed 12/16/2004 has been carefully considered, but is deemed not to be persuasive. The response argues that some inoperative embodiments encompassed by the scope of a claim does not necessarily make the claim nonenabled. The response argues that the specification at pages 47 and 53 and Examples 10-11, gives extensive guidance on the performance of the routine experiments required to determine whether just any variant peptide is functionally equivalent to the working embodiments disclosed and Tables 6 and 7 disclose that 41% (19 of 41) of the peptides tested stimulate CTL activity indicating that there is a reasonable expectation

that the skilled artisan would quickly distinguish operative from inoperative embodiments. In response to these arguments, the issue is not whether some embodiments encompassed by the claims are inoperable or whether one skilled in the art could distinguish operative embodiments from inoperative embodiments. The issue is whether or not undue experimentation would be required to practice the claimed invention commensurate in scope with the claims. The claims encompass a substantial number of variant sequences and the specification does not provide sufficient guidance or direction to assist the skilled artisan in the selection of the encompassed variant cancer peptides commensurate in scope with the claims. The specification does not teach any variant cancer peptide that includes amino acids 127-136 of SEQ ID NO:4. The specification only teaches the cancer peptide consisting of amino acids 127-136 of SEQ ID NO:4 (i.e., SEQ ID NO:15) (see Table 6). The specification provides no guidance or direction assisting the skilled artisan in the selection of cancer peptides that are 85% identical to SEQ ID NO:15 and have CTL activity. There is no disclosure of which amino acid residues are critical for CTL activity or which amino acid residues can be predictably modified or even which additional amino acid residues can be added to the N-terminus and retain the CTL activity of the parent cancer peptide (i.e., SEQ ID NO:15) with a reasonable expectation of success. The claims do not even require that the additional contiguous amino acids to be added to the N-terminus be contiguous N-terminal residues of the recited cancer peptide. For example, if the cancer peptide includes amino acids 55-62 of SEQ ID NO:4, the claims do not require that the additional amino acids at the N-terminus of this cancer peptide be amino acid residues

44-54 of SEQ ID NO:4. The specification at pages 47 and 53 and Examples 10-11 as pointed to by applicant essentially calls for the use of trial and error to attempt to find a cancer peptide that will stimulate CTL activity. Although some variant cancer peptides which include residues 55-62 of SEQ ID NO:4 are disclosed in Table 7, Table 7 evinces that not all variant cancer peptides will have the requisite CTL activity of the parent cancer peptide form which they were derived. Thus, without further guidance and direction in applicant's specification, one skilled in the art could not predictably produce and test each cancer peptide variant encompassed by the broad scope of the claims with a reasonable expectation of success without undue experimentation. The art of Falk and Missale only further illustrate that each and every cancer peptide variant would have to be tested for CTL activity and even minor changes in the peptide sequence results in loss of CTL activity (see Missale et al, Table 3).

A patent is not a reward for a search, but compensation for its successful conclusion. Reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. Applicant's arguments are not persuausive because as discussed above they are merely an invitation to the skilled artisan to experiment using the specification as a guide to determine for themselves which cancer peptide variants will work.

13. The rejection of claims 28-29 and 83-85 under 35 U.S.C. 102(a) as being anticipated by Chen et al is maintained.

The response filed 12/16/2004 has been carefully considered, but is deemed not to be persuasive. The response argues that claims 26 and 28 have been amended to make it clear that the disclosure of Chen et al is not encompassed by the subject matter of the claims. In response to this arguments, the claims are drawn to an immunogen comprising a composition comprising one or more..., the claim language "comprising" is open-ended and does not exclude additional unrecited elements. Therefore, the claims still encompass the full-length NY-ESO-1 sequence of Chen et al and thus, Chen et al anticipate the claims. The use of "consisting of" does not serve to limit the earlier term "comprising" especially in view that the claim recites "comprising one or more". See In re Crish, 73 USPQ2d 1364 (CA FC 2004).

Conclusions

14. No claim is allowed. Claims 89-91 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. In rewriting the claims, applicant is advised that part (vi) of claim 88, i.e., amino acids 43-62 of SEQ ID NO:4 currently stand rejected for new matter and the generic claim language with respect to parts (xi) and (xii) of claim 88 also stand rejected for lack of enablement and new matter.

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827

LARRY R. HELMS, PH.D
PRIMARY EXAMINER